Paper No. 23

# UNITED STATES PATENT AND TRADEMARK OFFICE

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# BEFORE THE BOARD OF PATENT APPEALS AND INTERFERENCES

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Ex parte SERENGULAM V. GOVINDAN and GARY L. GRIDDITHS

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Appeal No. 2001-0758
Application No. 08/919,477

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HEARD: March 19, 2002

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Before WILLIAM F. SMITH, SCHEINER and GREEN, Administrative Patent Judges.

SCHEINER, Administrative Patent Judge.

VACATUR AND REMAND TO THE EXAMINER

Our consideration of the record leads us to conclude that this case is not in condition for a decision on appeal. While we are reluctant to remand this application to the examiner at this late date, by statute, this board functions as a board of review.[1] Here, we are faced with a record that is not susceptible to meaningful review. Accordingly, we vacate [2] the examiner's rejection and remand the application to the examiner to consider the following issues and take action not inconsistent with the views expressed in the following opinion.

Claims 1, 2, 7, 8 and 19 are representative of the subject matter at issue:

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[1] 35 U.S.C. § 6 (b) states that "[t]he [board] shall . . . review adverse decisions of examiners upon applications for patents . . ."

[2] The term "vacate" means to set aside or void. Black's Law Dictionary 1075 (abridged 6th ed. 1991). When the board vacates a rejection and remands the application to the examiner, that rejection no longer exists, the appeal is ended and jurisdiction over the application on appeal is returned to the examiner for further action not inconsistent with the views expressed in the opinion accompanying the board's decision. See also Ex parte Zambrano, 58 USPQ2d 1312 (Bd.Pat.App. & Int. 2001).

1. An aminopolycarboxylate-appended peptide useful for radioiodinating an antibody, comprising:

(a) a peptide that comprises at least one D-tyrosine or tyramine, an amino terminus, a carboxy terminus formed from a D-lysine and no contiguous L-amino acids between the D-tyrosine or tyramine and the carboxy terminus;

(b) an aminopolycarboxylate conjugated via one of its carboxylic acid groups to the peptide via an ϵ-amino group of the D-lysine to form an aminopolycarboxylate-appended peptide; and

(c) a linker group for covalently binding said aminopolycarboxylate-appended peptide to an antibody.

2. The aminopolycarboxylate-appended peptide of claim 1, further comprising a radioiodine atom covalently bound to the D-tyrosine or tyramine residue.

7. Tha aminopolycarboxylate-appended peptide of claim 1, wherein said aminopolycarboxylate is selected from the group consisting of nitrilotriacetic acid, EDTA, DTPA, TTHA, and backbone-substituted derivatives of nitrilotriacetic acid, EDTA, DTPA, TTHA.

8. An aminopolycarboxylate-appended peptide useful for radioiodinating an antibody, comprising:

(a) a peptide that comprises at least one D-tyrosine or tyramine, an amino terminus, a carboxy terminus formed from a D-amino acid and no contiguous L-amino acids between the D-tyrosine or tyramine and the carboxy terminus;

(b) an aminopolycarboxylate conjugated via one of its amino groups to the peptide via an amide bind to a peptide carboxylic acid group or via a thiourea bond to a peptide amino acid residue to form an aminopolycarboxylate-appended peptide; and

(c) a linker group for covalently binding said aminopolycarboxylate-appended peptide to an antibody.

19. The aminopolycarboxylate-appended peptide of claim 1, wherein said linker is selected from the group consisting of an amino group, imidate group, isothiocyanate group, maleimide group and halo-acetamide group.

The references relied on by the examiner are:

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| Barbet et al. (Barbet) | 5,274,076 | Dec. 28, 1993 |
| Matthews et al (Matthews) | 5,273,738 | Dec. 28, 1993 |

Adams et al. (Adams) GB 2 109 407 Jun. 2, 1983

DISCUSSION

The issue appellants would have us review is whether claims 1 through 9, 19 and 20 are unpatentable under 35 U.S.C. § 103 over Barbet, Adams and Matthews. Unfortunately, our review of this matter has been hampered by the failure of the examiner to address the claims on an individual basis, and even more so by the inconsistent manner in which the examiner has treated an express limitation of the claims.

Claim 1 is directed to an aminocarboxylate-appended peptide comprising "at least one D-tyrosine or tyramine, an amino terminus, a carboxy terminus formed from D-lysine and no contiguous L-amino acids between the D-tyrosine or tyramine and the carboxy terminus," with "an aminopolycarboxylate conjugated to the ϵ-amino group of the D-lysine through one of its carboxylic acid groups," and "a linker group for covalently binding [the peptide] to an antibody." Claim 8 is similar to claim 1, except that the aminopolycarboxylate is conjugated to the peptide through an amide bond or a thiourea bond. Claims 19 and 20, which depend from claims 1 and 8, respectively, specify that the linker group consists of an amino group, an imidate group, an isothiocyanate group, a maleimide group or a halo-acetamide group.

Barbet describes several molecules "compris[ing] two hydrophilic haptens and an effector group comprising a radioactive isotope" (including isotopes of iodine) wherein the haptens are joined by a peptidyl "connecting bridge[ ] . . . which allow[s] adequate separation of haptens" and which is "not very sensitive to hydrolysis." Column 1, lines 43-45; column 2, lines 63-67; and column 4, lines 15-18. One such molecule is N-α-DTPA-tyrosyl-N-ϵ-DTPA-lysine - thus Barbet describes an aminopolycarboxylate-

appended peptide with tyrosine at the amino terminus, lysine at the carboxy terminus (with no amino acid residues at all between them), and an aminopolycarboxylate (DTPA) conjugated to the ϵ-amino group of lysine via one of its carboxylic acid groups. Moreover, Barbet explicitly suggests that a connecting bridge containing "one or several D-amino acids [is] preferred." Column 4, lines 9-10.

That being the case, we agree with the examiner to the extent that he concludes that Barbet "would render obvious [radioiodinated] N-alpha-DTPA-Tyr-N-epsilon-DTPA-lysine containing D-amino acids and additionally . . . peptides . . . [wherein] Tyr is separated from Lys by one or more D-amino acids." Answer, page 4.

Nevertheless, claims 1-9 broadly require "a linker group for covalently binding [the] aminopolycarboxylate-appended peptide to an antibody." That is, even though there is no requirement that the aminopolycarboxylate-amended peptide be covalently bound to an antibody, it must contain a linker capable of doing so (stated another way, the peptide need only contain a linker capable of covalently binding an antibody). It is the examiner's treatment of this limitation that gives rise to our difficulties in reviewing the rejection at issue.

In the final rejection, apparently with respect to the "linker" limitation, the examiner explicitly concedes that "the Barbet reference teaching of a 'hapten' ([ ] e.g. DTPA) attached to a D/L Tyr containing peptide fails to anticipate or render obvious (by itself) the . . . invention of claims 1 and 8 (and claims dependent thereon)" (Final Rejection, Paper No. 10, page 4). However, in responding to appellants' argument in the Brief that Barbet fails to disclose the required linker, the examiner retracts that concession, asserting that appellants are "misguided in this respect" as "the linker limitation is met by the other DTPA present in [Barbet's] compound (e.g. N-alpha

DTPA)." Answer, pages 8 and 9. It is not clear what the basis for the examiner's assertion is, and the actual statement of the rejection (Answer, pages 4-7) says nothing about the broad linker limitation,[3] focusing instead on the limitations of narrower claims 19 and 20. The last word on this issue is appellants' blanket assertion in the Reply Brief (page 3), that "Barbet does not teach or suggest a [linker] group for covalent attachment to an antibody."

The findings of fact underlying an obviousness rejection, as well as conclusions of law, must be made in accordance with the Administrative Procedure Act, 5 U.S.C. 706 (A),(E) (1994). See Zurko v. Dickinson, 527 U.S. 150, 158, 119 S.Ct. 1816, 1821, 50 USPQ2d 1930, 1934 (1999). Findings of fact underlying the obviousness rejection must be supported by substantial evidence within the record. See In re Gartside, 203 F.3d 1305, 1315, 53 USPQ2d 1769, 1775 (Fed. Cir. 2000). In addition, in order for meaningful appellate review to occur, the examiner must present a full and reasoned explanation of the rejection. See, e.g., In re Lee, 277 F.3d 1338, 1342, 61 USPQ2d 1430, 1432 (Fed. Cir. 2002). We would further emphasize what should be self-evident: the examiner must present a full and reasoned explanation of the rejection in the statement of the rejection, specifically identifying underlying facts and any supporting evidence, in order for appellants to have a fair and meaningful opportunity to respond. Clearly, the examiner's rejection does not meet this standard, but we are reluctant to simply reverse the examiner's decision on this basis alone.

In our view, the examiner's belated assertion that "[t]he linker limitation is met by [Barbet's N-alpha] DTPA" (Answer, page 9), "which can act as a linking group" (Answer,

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[3] We note that the examiner uses the phrase "peptide linker" in the statement of the rejection, but in every case, the phrase refers to the peptidyl portion of Barbet's aminopolycarboxylate-appended peptide, not to any "linker group" within the meaning of the claims at issue.

page 20) is at least superficially plausible, inasmuch as the claims merely require a "linker group" capable of covalently binding an antibody; Barbet shows that DTPA is capable of forming a covalent bond, through a carboxylic acid group, with an amino acid residue; and DTPA has multiple carboxylic acid groups. Nevertheless, as this issue was never raised in the examiner's statement of the rejection, we cannot say with any confidence that appellants have had any real opportunity to respond.

Accordingly, we vacate the examiner's rejection and remand the application to the jurisdiction of the examining group for consideration of this issue. We emphasize that our action today terminates the appeal process, and we are not authorizing a supplemental examiner's answer under 37 CFR § 1.193(b)(1).

FUTURE PROCEEDINGS

Should the examiner choose to issue a new office action in this case, we point out the following deficiencies in one of the principal positions taken in the examiner's Answer. The examiner asserts that Barbet "clearly suggests the covalent attachment of [ ] antibody(ies) to the Barbet aminopoly-carboxylate-appended peptides via a linker group (e.g. one or both DTPA groups)" (Answer, page 10), while Adams "discloses the use of linkers (e.g., maleimide, isothiocyanate . . . [etc.]) to attach a polyaminocarb-oxylic (e.g. chelating agent) to an antibody" (Id., page 6), and concludes that "it would have been obvious . . . to utilize a linker, as disclosed in [Adams], to modify the Barbet aminopolycarboxylate-appended peptides for attachment of antibody in order to obtain a tumor diagnostic probe as suggested by [ ] Barbet" (Id.). We cannot agree with the examiner's analysis or conclusion.

The problem with the examiner's rationale is that there is absolutely nothing in Barbet to suggest the desirability of a covalent attachment between an antibody and the

aminopolycarboxylate-appended peptide. Barbet describes two separate diagnostic or therapeutic reagents designed to work together upon simultaneous or sequential injection. The first reagent is a bivalent conjugate "comprising an antibody . . . having an affinity for a particular cell type . . . coupled to an antibody . . . having an affinity for a given hapten." Barbet, column 6, lines 4-10. The second is "a synthetic molecule comprising at least two haptens and [ ] at least one site, suitable for radioactive labelling bound in covalent manner." Id., column 6, lines 10-14. An example of this second reagent is the aminopolycarboxylate-appended peptide, N-α-DTPA-tyrosyl-N-ϵ-DTPA-lysine, discussed above. The first reagent binds its target cell through the antibody "having an affinity for a particular cell type," and also binds the second reagent through the antibody "having an affinity for a given hapten." In our view, the only reasonable interpretation of the reference is that the bond between the hapten-specific antibody of the first reagent and the hapten of the second reagent is a non-covalent immunospecific interaction "at the level of one of [the antibody's] binding sites." Barbet, column 1, line 52.

Under these circumstances, we see no nexus between Barbet and Adams - thus, we see no basis for the examiner's conclusion that "it would have been obvious . . . to utilize a linker, as disclosed in [Adams], to modify the Barbet aminopolycarboxylate-appended peptides."

## CONCLUSION

As stated above, this board serves as a board of review, rather than a de novo examination tribunal (35 U.S.C. § 6(b)). Here, we find that the incomplete, inconsistent analysis of the claims, and the inaccurate analysis of the prior art, preclude meaningful review. Accordingly, we vacate the rejection of record and remand the case to the

examiner so that a new decision can be made based on all relevant facts, prior art and objective evidence. We are not authorizing a supplemental examiner's answer under 37 CFR § 1.193(b)(1), and any future communication from the examiner that contains a rejection of the claims should provide appellants with a full and fair opportunity to respond.

VACATED AND REMANDED

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| William F. Smith<br>Administrative Patent Judge | ) |
| Toni R. Scheiner<br>Administrative Patent Judge | ) BOARD OF PATENT<br>) APPEALS AND<br>) INTERFERENCES |
| Lora M. Green<br>Administrative Patent Judge | ) |

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